REMARKS

In the Office Action dated March 9, 2004, Claims 4-12, 14-37 and 45-49 are pending. Claims 16-24, 28, 30-37 have been withdrawn from consideration as drawn to non-elected embodiments. Claims 4-12, 14-15, 25-27, 29 and 45-49 are under consideration. Claims 4-12, 14-15, 25-27, 29 and 45-49 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting, as allegedly unpatentable over claims 13-15 and 20 of copending application, Serial No. 10/616,682. Claims 4-12, 14-15, 25-27, 29 and 45-49 are rejected under 35 U.S.C. §112, first paragraph, as allegedly lacking enablement. The Examiner has also objected to the priority claim made by Applicant.

This Response addresses each of the Examiner's rejections and objections. Applicant therefore respectfully submits that the present application is in condition for allowance. Favorable consideration of all pending claims is therefore respectfully requested.

In the Office Action, the Examiner alleges that Applicant has not addressed the issue of priority or provided copies of the priority documents.

Contrary to the Examiner's allegation, certified copies of the priority documents, Australian Provisional Applications PR1327 and PQ8242, were submitted with the Response dated December 4, 2003. In addition, Applicant stated in the Response of December 4, 2003, that certified copies of the priority documents were enclosed thereby perfecting the Applicant's priority claim.

In the claims, Applicant has canceled claims 4-12, 14-37 and 45-49 without prejudice, and has added claims 50-67 to more clearly delineate preferred embodiments of the present application. In particular, in the new claims, the progenitor cells and ES cells are human

progenitor cells and human ES cells. Support for claims 50-67 is found throughout the specification and in the original claims. No new matter is added.

The Examiner has provisionally rejected claims 4-12, 14-15, 25-27, 29 and 45-49 under the judicially created doctrine of obviousness-type double patenting, as allegedly unpatentable over claims 13-15 and 20 of copending application, Serial No. 10/616,682. The Examiner contends that, although the conflicting claims are not identical, they are not patentably distinct from each other.

Applicant respectfully submits that the rejection is rendered moot in view of the cancellation of the claims. It is also believed that new claims 50-67, reciting human progenitor cells and human ES cells, are patentably distinct from the claims of the '682 application. In any event, it is observed that the '682 application has not issued. Therefore, Applicants respectfully request withdrawal of the double patenting rejection based on the '682 application.

Claims 4-12, 14-15, 25-27, 29 and 45-49 are rejected under 35 U.S.C. §112, first paragraph, as allegedly lacking enablement.

The Examiner acknowledges that the specification is enabling for methods of culturing human embryonic stem (ES) cells comprising obtaining a source of human ES cells, and culturing the human ES cells in the presence of noggin for five days thereby resulting in an undifferentiated cell which does not express ES stem cell markers. However, the Examiner alleges that the specification does not provide enablement for methods using the ES cells of any species of animal or for producing progenitor cells as claimed.

The rejection is rendered moot in view of cancellation of these claims.

Applicant further respectfully submits that in new claims 50-67, the ES cells are human ES cells. Applicant reserves the right to pursue the methods of culturing embryonic stem (ES) cells from species other than human in a continuing/divisional application.

The Examiner seems to suggest that the ES cells are cultured for five days in order to obtain the intermediate cell type. Applicant respectfully submits that based on the present teaching, those skilled in the art would be able to determine when an intermediate cell type has been developed by observing the loss of stem cell markers, which does not necessarily coincide with 5 days. The specification clearly teaches that an intermediate cell type can be induced with noggin, and that such intermediate cell type falls somewhere between the undifferentiated and fully differentiated state. As described in the specification on pages 13-14, such intermediate cell type can be identified by observing the change in cell morphology and detecting the loss of at least one ES cell marker, such as those listed in the paragraph bridging page 13-14. As stated in the specification, the time period of 5 days is only approximate. See page 13, line 11 and page 27, line 21. The loss of an ES cell marker may occur at a time that is not precisely five days, but certainly can be determined by those skilled in the art without undue experimentation.

Accordingly, Applicant respectfully submits that the methods, as presently claimed, are fully enabled by the specification. Withdrawal of the rejection under 35 U.S.C. §112, first paragraph, is therefore respectfully requested.

Claims 14-15 and 29 are rejected under 35 U.S.C. §102(b) as allegedly anticipated by Thomson (US Patent 5,843,780). Claims 14-15 and 29 are drawn to progenitor cells and undifferentiated cells produced from undifferentiated ES cells treated with an antagonist of a BMP mediated default pathway.

The Examiner contends that Thomson teaches primate embryonic stem cells, which are pluripotent and capable of giving rise to the various somatic cell lineages. The Examiner is of the opinion that the claimed cells are identical or substantially identical to those disclosed by Thomson. Specifically, the Examiner states that, although the presently claimed cells are produced by culturing ES cells in the presence of noggin, the present claims do not set forth any particular effect of noggin on the cultured ES cells. Therefore, the Examiner states that the undifferentiated ES cells and progenitor cells, as presently claimed, are interpreted to be cells capable of giving rise to any cell type of any lineage, indistinguishable from cells taught by Thomson.

Applicant respectfully submits that claims 14-15 and 29 have been canceled, rendering the rejection moot. Applicant further respectfully submits that new claims 57 and 66-67 are drawn to a human progenitor cell derived from an undifferentiated human ES cell, wherein said progenitor cell lacks at least one marker of said undifferentiated ES cell.

Applicant respectfully submits that Thomson does not teach a human progenitor cell derived from an undifferentiated human ES cell. Thomson merely teaches the preparation and culturing of primate ES cells in general, and has only illustrated the use of non-human primates, namely the common marmoset and the rhesus monkey. Thomson does not teach a human ES cell, let alone a progenitor cell produced from a human ES cell cultured in the presence of an antagonist of a BMP mediated default pathway, such as noggin. Furthermore, as the Examiner has admitted in the context of the enablement issue, it is known in the art that ES cells differ from species to species; in particular, human ES cells differ in the *in vitro* requirements as compared to ES cells from mouse, rat and hamsters, among others. (See page 11 of the Office

Action.) Accordingly, the disclosure in Thomson relating to a primate ES cell is inadequate to anticipate the human progenitor cell produced from a human ES cell, as presently claimed.

Applicant further respectfully submits that the progenitor cell, as presently claimed, lacks at least one marker of the undifferentiated human ES cell. As the Examiner has stated in the Office Action, Thomson teaches primate embryonic stem cells, which are pluripotent. These pluripotent ES cells are not expected to lack "at least one marker of the undifferentiated ES cell", as presently claimed.

Accordingly, it is respectfully submitted that Thomson does not teach the progenitor cell, as presently claimed. Withdrawal of the rejection based on Thomson is therefore respectfully requested.

Claims 14-15 and 29 are also rejected under 35 U.S.C. §102(e) as allegedly anticipated by Carpenter et al. (US2002/0019046 A1).

Applicant respectfully submits that the rejection is rendered moot in view of the cancellation of claims 14-15 and 29. Applicant respectfully submits the following insofar as the rejection may be applicable to new claims 57 and 66-67 which are drawn to progenitor cells.

It is observed that in Carpenter et al., human embryonic stem cells (hES) have been differentiated to precursor cells. Carpenter et al. also teach treating cultured human ES cells with combinations of factors, such as the combination noggin and follistatin.

Applicant first respectfully submits that the markers used to characterize the precursor cells in the Carpenter application are not the same as those used to identify the progenitor cells, as claimed in the present application. The present progenitor cells, which are derived from human ES cells treated with an antagonist of a BMP mediated default pathway of extra embryonic endoderm differentiation (such as noggin), are further characterized by being

unreactive with any one of the antibodies outlined in claims 58 and 67. None of those markers are identified in the Carpenter application. It is believed that by virtue of different markers, the presently claimed progenitor cells are distinct from the precursor cells disclosed by Carpenter et al.

Applicant further respectfully submits that the present progenitor cells are produced by culturing human ES cells with an antagonist of BMP-mediated default pathway of extraembryonic endoderm differentiation, preferably noggin. The progenitor cells, as presently claimed, were first identified in the priority document, PR1327, filed on November 8, 2000. In PR1327, the use of noggin to produce progenitor cells is described.

It is observed that the Carpenter application (US2002/0019046) claims priority from three priority documents, namely

1. US6O/21 3.739 filed on 22 June 2000
2. US60121 6,387 filed on 7 July 2000
3. US6O/220,064 filed on 21 July 2000.

However, the disclosure by Carpenter et al. with respect to the use of noggin for producing precursor cells only first appears in Carpenter's application, filed on June 21, 2001, published as US2002/0019046A1. Accordingly, the progenitor cells prepared by a process involving an antagonist of BMP-mediated default pathway such as noggin, as presently claimed, has not been disclosed by Carpenter et al. before the priority date of the present application. The progenitor cells as presently claimed are distinct from precursor cells prepared by a process without the use of an antagonist of BMP-mediated default pathway such as noggin. Therefore, it is respectfully submit that Carpenter et al. do provide adequate teaching that would anticipate the claimed progenitor cells under §102(e).

Accordingly, the rejection based on Carpenter et al. under 35 U.S.C.§102(e) is overcome. Withdrawal of the rejection is therefore respectfully requested.

In view of the foregoing amendments and remarks, it is firmly believed that the subject application is in condition for allowance, which action is earnestly solicited.

Respectfully submitted,

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